(3) The frequency and amplitude of the neural activity recorded from the SLGP, LSG and RSN were markedly increased by 1 hour intermittent hypoxia.
(4) EMF reversed all these changes induced by 1 hour intermittent hypoxia.

CONCLUSIONS EMF suppressed AF inducibility and the responses to SLGP and LSG stimulation induced by intermittent hypoxia. Inhibition of neural activities in the GP, LSG and RSN may be a mechanism underlying these results.

GW26-e2307

Acute and chronic effects of acehytisine on sodium channel in primary rat atrial myocytes

Xinrong Fan,[1,2] Chao Wang,[2] Mengmeng Yang,[2] Xiaorong Zeng,[1] Hanxiong Liu,[2] Lin Cai[2]
[1]The Institute of Cardiovascular Research, Luzhou Medical College, Luzhou, China; [2]Department of Cardiology, Institute of Cardiovascular Disease of Chengdu, the Third People's Hospital of Chengdu, Chengdu, China

OBJECTIVES Acehytisine (previously named Guanfu base A), a novel diterpene alkaloid isolated from the root of aconitum coreanum (Levl.) raipaics which has been shown to effectively terminate AF and supraventricular tachycardia in patients and animal models by blocking multi-ion channels, but its effects on cellular electro pharmacological activities of sodium channels are largely unknown in atrial myocytes.

METHODS Primary atrial myocytes were isolated and cultured from neonatal Sprague-Dawley rats (born 1-2 days). A single-pipette whole-cell patch-clamp was used to investigate the acute effect of acehytisine on sodium channels, and RT-PCR and western blot were used to quantify α and β-subunits mRNA and protein expression implied chronic effect on sodium channels.

RESULTS Atrial myocytes were cultured and plated into coverlips at $1\times10^4/cm^2$. 48h later, single cell was ruptured and I_{Na} was recorded in absence and presence of acehytisine. It inhibited I_{Na} in a positive rate-dependent and concentration-dependent manner, with IC_{50} value of 31.67±5.47μmol/L. 50μmol/L acehytisine significantly shifted inactivation curves toward left and shifted activation curves to right, but did not modify the recovery kinetics from inactivation of sodium channels. In addition, incubation with 100μmol/L acehytisine for 3-24h caused significant decreases of α and β-subunits mRNA in time-dependent manner (SCN5A decreased by 72.24±18.21%, SCN1B decreased by 52.81±19.77%, SCN3B decreased by 83.42±35.16% at 24h, $p<0.01$ vs. untreated cells). Meanwhile, the quanification of protein levels was consistent with alteration of mRNA expression.

CONCLUSIONS These findings indicate that acehytisine inhibits sodium channels by two modes, 1) inhibiting I_{Na} by binding to sodium channels and 2) downregulating α and β-subunits at mRNA and protein levels, which provides experimental evidence for anti-arrhythmia by acehytisine.

GW26-e2401

Enhanced levels of miR-122-5p and let-7b-3p in aortas of spontaneously hypertensive rats associated with downregulated levels of Apelin, miR-1-3p, miR-376b-3p and miR-298-5p

Jiuchang Zhong,[1,2] Ran Xu,[1,2] Laijiang Chen,[1,2] Zhenzhou Zhang,[1,2] Yingle Xu,[1] Qing Chang,[1] Dingliang Zhu,[1,2] Pingjin Gao[1,2]
[1]State Key Laboratory of Medical Genomics, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai Institute of Hypertension, China; [2]Institute of Health Sciences, Shanghai Institute for Biological Sciences, Chinese Academy of Sciences, China

OBJECTIVES The deregulation of microRNAs (miRNAs), a class of short and small non-coding RNAs, has been shown to be involved in a wide range of cellular processes and cardiovascular pathologies. The Apelin/APJ system has been implicated in the pathophysiology effects in cardiovascular system, which is a necessary process in the initiation and development of various cardiovascular diseases inclusive of hypertension. We hypothesized that Apelin is a negative regulator of hypertension-mediated pathological effects in spontaneously hypertensive rats (SHR) model.

METHODS The 3-month-old male SHR and Wistar-Kyoto (WKY) rats were obtained from Slac Laboratory Animal Co. Ltd. in China. Rats received daily administration of Apelin or saline for 4 weeks. Systolic blood pressure (SBP) of rat was measured by the tail-cuff method. Vascular morphological analysis was processed using the computer image analysis software for the quantification of the media thickness (MT), lumen diameter (LD), and the ratio of MT to LD, markers of vascular hypertrophy and remodeling.

RESULTS In the SHR model, the aortic expression of miR-122-5p and let-7b-3p were upregulated, while miR-1-3p, miR-376b-3p and miR-298-5p were downregulated and negative correlated with SBP levels. Compared with WKY rats, the MT and the MT/LD ratio of the thoracic aorta were significantly enhanced in SHR [MT: (127.2±4.5 um) vs.(81.8±3.9 um); MT/LD ratio:(7.3±1.1) vs.(4.8±1.0); $P<0.01$, respectively]. These changes were linked with the reduction of Apelin expression and increased levels of ANF, and phosphorylated ERK1/2 as well as severe ultrastructural damage of the thoracic aorta. These effects were significantly blunted by Apelin treatment, in association with a lowering of phosphorylated ERK1/2 levels and improvement of ultrastructural injury. However, there were no changes in aortic expression of APJ receptor among groups.

CONCLUSIONS There are abnormal levels of miRNAs and Apelin in hypertensive status. In addition, Apelin is an important negative regulator of the hypertension-induced pathological hypertrophy and aortic remodeling and attenuates aortic ultrastructural injury in hypertensive rats. These observations indicate that various miRNAs and Apelin signaling in vasculature may be linked with hypertension and provide novel pharmacologic implications for the prevention and treatment of hypertension.

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The Expression of Ubc9 and the Intensity of SERCA2a-SUMOylation Were Reduced in Diet-induced Obese Rats and Partially Restored by Trimetazidine

Jing Yao,[1] Tian-Chang Li,[1] Xing-Hui Shao,[2] Zheng-Ming Xu,[1] Meng-Yue Yu,[2] Si-Yong Teng,[2] Yong-Jian Wu[2]
[1]Navy General Hospital, People's Liberation Army; [2]Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES Reduced expression of Sarcoplasmic reticulum calcium-transporting ATPase isoform 2a (SERCA2a) has been shown to play a significant role in the cardiac dysfunction of obese animal models. It was reported recently that SUMOylation enhances the stability and activity of SERCA2a. We hypothesized that SERCA2a-SUMOylation might be involved in obesity-mediated reduction of SERCA2a.

METHODS Trimetazidine (TMZ), the drug that inhibits fatty acid oxidation, was used in diet-induced obesity (DIO) rats and palmitic acid (PA)-treated cardiomyocytes. The intensity of SERCA2a-SUMOylation and proteins involved in SERCA2a-SUMOylation were investigated in vivo and in vitro.

RESULTS DIO rats presented cardiac dysfunction, which was alleviated by TMZ treatment. Reductions of SERCA2a protein and the intensity of SERCA2a-SUMOylation were observed in DIO rats and PA-treated cardiomyocytes. These reductions were partially restored by TMZ. However, TMZ itself did not alter the intensity of SERCA2a-SUMOylation in control cardiomyocytes. The variations of protein and mRNA levels of Ubc9 are in accordance with the intensity of SERCA2a-SUMOylation. Whereas the other proteins involved in SERCA2a-SUMOylation were not changed by DIO and PA.

CONCLUSIONS TMZ alleviates the DIO-induced and PA-induced reductions of SERCA2a-SUMOylation. Ubc9 is involved in the reductions.

GW26-e4628

Assessment of osteopontin, osteoprotegerin and activated monocytes/macrophages on hypertensive patients with vascular calcification

Qian Ge,[1,2] ChengChao Ruan,[2] Yu Ma,[2] QiHong Wu,[2] JiGuang Wang,[1,2] DingLiang Zhu,[1,2] Pinjing Gao[1,2]
[1]Department of Hypertension, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine; [2]Shanghai Institute of Hypertension

OBJECTIVES Vascular calcification (VC) is a highly regulated process in which inflammatory cells infiltration and the factors controlling bone mineralization are involved. This study aims to examine whether osteopontin (OPN) and osteoprotegerin (OPG) exert effects in hypertensive subjects with VC by regulating monocyte/macrophage activation.

METHODS We recruited 70 hypertensive subjects with or without VC by artery electronic calculator tomography, peripheral blood monocytes (CD14+) and primary cultured macrophages were detected